

In the Claims

Please cancel Claims 3, 24, 29, 32, 33, 41, 50 and 51.

Please amend Claims 1, 2, 9, 12, 23, 27, 28, 30, 35 and 49. Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i - v).

1. (Thrice Amended) A recombinant vector comprising, in operable linkage,

- a) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- b) one or more coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepromelittin, cecropin, prececropin, preprocerecropin, magainin, a part thereof, an analogue thereof, a homologue thereof and a combination thereof.

2. (Thrice Amended) The recombinant vector according to Claim 1 comprising in operable linkage,

- a) a 5' long terminal repeat region comprising the structure U3-R-U5;
- b) one or more of said coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepromelittin, cecropin, prececropin, preprocerecropin, magainin, a part thereof, an analogue thereof, a homologue thereof and a combination thereof; and
- c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence, followed by the R and U5 region to undergo promoter conversion.

9. (Thrice Amended) A recombinant retroviral vector system comprising:

- a) a recombinant vector comprising, in operable linkage,

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- i) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- ii) one or more coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepromelittin, cecropin, prececropin, preprocropin, magainin, a part thereof, an analogue thereof, a homologue thereof and a combination thereof; and

b) a packaging cell line harboring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.

12. (Amended) A retroviral provirus produced by infection of target cells with a recombinant retroviral particle according to Claim 11 whereby the U3 sequence is duplicated during the process of reverse transcription in the infected target cell and appears in the 5' long terminal repeat and the 3' long terminal repeat of the resulting provirus, and the U5 of the 5' long terminal repeat is duplicated during the process of reverse transcription in the infected target cell and appears in the 3' long terminal repeat and in the 5' long terminal repeat of the resulting provirus.

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23. (Thrice Amended) A method for the treatment of a disease selected from the group consisting of: a genetic defect, cancer and viral infections, comprising administering to a subject in need thereof a therapeutically effective amount of a recombinant retroviral particle produced by transfecting a packaging cell line harboring at least one retroviral or recombinant retroviral construct coding for proteins required for said retroviral vector to be packaged, with a recombinant retroviral vector comprising, in operable linkage,
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a) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
b) one or more coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active

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derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepromelittin, cecropin, prececropin, preprocercropin, magainin, a part thereof, an analogue thereof, a homologue thereof and a combination thereof.

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27. (Amended) A recombinant vector comprising, in operable linkage,

- retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- one or more coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepromelittin, a part thereof, an analogue thereof, a homologue thereof, and a combination thereof.

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28. (Amended) The recombinant vector according to Claim 27 comprising in operable linkage,

- a 5' long terminal repeat region comprising the structure U3-R-U5;
- one or more of said coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepromelittin, a part thereof, an analogue thereof, a homologue thereof, and a combination thereof; and
- a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence, followed by the R and U5 region to undergo promoter conversion.

30. (Amended) The recombinant vector according to Claim 28, wherein said polylinker sequence comprises at least one unique restriction site and, optionally, at least one insertion of a heterologous DNA fragment.

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35. (Amended) A recombinant retroviral vector system comprising:

- a) a recombinant vector comprising, in operable linkage,
 - i) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
 - ii) one or more coding sequences wherein at least one sequence encodes for at least one naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepromelittin, a part thereof, an analogue thereof, a homologue thereof, and a combination thereof; and
- b) a packaging cell line harboring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.

49. (Amended) A method for the treatment of a disease selected from the group consisting of: a genetic defect, cancer and retroviral infections, comprising administering to a subject in need thereof a therapeutically effective amount of a recombinant retroviral particle produced by transfecting a packaging cell line harboring at least one retroviral or recombinant retroviral construct coding for proteins required for said retroviral vector to be packaged, with a recombinant retroviral vector comprising, in operable linkage,

- a) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- b) one or more coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepromelittin, a part thereof, an analogue thereof, a homologue thereof, and a combination thereof.

Please add new Claims 53-77 shown below.

53. (New) A method for treatment of a cancer, comprising administering to a subject in need thereof a therapeutically effective amount of a recombinant retroviral vector comprising, in operable linkage,

- retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- one or more coding sequences wherein at least one sequence encodes for at least one naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepromelittin, cecropin, prececropin, procecropin, magainin, a part thereof, an analogue thereof, a homologue therefor and a combination thereof.

54. (New) A method for treatment of a viral infection, comprising administering to a subject in need thereof a therapeutically effective amount of a recombinant retroviral vector comprising, in operable linkage,

- retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- one or more coding sequences wherein at least one sequence encodes for at least one naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepromelittin, cecropin, prececropin, procecropin, magainin, a part thereof, an analogue thereof, a homologue therefor and a combination thereof.

55. (New) A recombinant vector comprising, in operable linkage,

- retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- one or more coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active



derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: cecropin, prececropin, preprocerecropin, SB-37, Shiva-1, a part thereof, an analogue thereof, a homologue thereof, and a combination thereof.

56. (New) The recombinant vector according to Claim 55 comprising in operable linkage,

- a 5' long terminal repeat region comprising the structure U3-R-U5;
- one or more of said coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: cecropin, prececropin, preprocerecropin, a part thereof, an analogue thereof, a homologue thereof, and a combination thereof; and
- a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence, followed by the R and U5 region to undergo promoter conversion.

57. (New) The recombinant vector according to Claim 56, wherein said polylinker sequence comprises at least one unique restriction site and, optionally, at least one insertion of a heterologous DNA fragment.

58. (New) The recombinant vector of Claim 57 wherein said heterologous DNA fragment regulates the expression of at least one of the coding sequences of said retroviral vector, and comprises at least one or more elements selected from the group consisting of: regulatory elements and promoters.

59. (New) The recombinant vector according to Claim 57, wherein said heterologous DNA fragment encodes a peptide selected from the group consisting of marker peptides, therapeutic peptides, cell cycle regulatory peptides, tumor suppressor peptides, antiproliferation peptides and cytokines.

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60. (New) A recombinant retroviral vector system comprising:

- a) a recombinant vector comprising, in operable linkage,
 - i) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
 - ii) one or more coding sequences wherein at least one sequence encodes for at least one naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: cecropin, prececropin, preprocecropin, a part thereof, an analogue thereof, a homologue thereof, and a combination thereof; and
- b) a packaging cell line harboring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.

61. (New) The recombinant retroviral vector system according to Claim 60, wherein said retroviral vector comprises, in operable linkage,

- a) a 5' long terminal repeat region comprising the structure U3-R-U5;
- b) one or more of said coding sequences; and
- c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence, followed by the R and U5 region to undergo promoter conversion.

62. (New) A retroviral particle produced by the recombinant retroviral vector system according to Claim 60 after transfecting the packaging cell line with the retroviral vector system.

63. (New) A retroviral provirus produced by infection of target cells with a recombinant retroviral particle according to Claim 62 whereby the U3 sequence duplicated during the process of reverse transcription in the infected target cell and appears in the 5' long terminal repeat and the 3' long terminal repeat of the resulting provirus, and the U5 of the 5' long terminal repeat duplicated during the process of reverse transcription in the

infected target cell and appears in the 3' long terminal repeat and in the 5' long terminal repeat of the resulting provirus.

64. (New) The retroviral provirus of Claim 63 wherein said polylinker comprises heterologous DNA.
65. (New) A method for introducing nucleotide sequences into an isolated cell population comprising infecting the cell population with the recombinant retroviruses produced by the recombinant retroviral vector system according to Claim 60.
66. (New) A method for introducing nucleotide sequences into a mammal comprising infecting the mammal with the recombinant retroviruses produced by the recombinant retroviral vector system according to Claim 60.
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67. (New) A method of treating an individual having at least one disease selected from the group consisting of: tumors and retroviral infections, comprising administering the recombinant vector of Claim 55 to the individual.
68. (New) A method of treating an individual having at least one disease selected from the group consisting of: tumors and retroviral infection, comprising administering the recombinant vector of Claim 60 to the individual.
69. (New) A pharmaceutical composition containing a therapeutically effective amount of a recombinant retroviral particle according to Claim 62.
70. (New) mRNA of a retroviral provirus according to Claim 63.
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71. (New) RNA of a vector according to Claim 60.
72. (New) An isolated host cell infected with a virion according to Claim 62.

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73. (New) A method for the treatment of a disease selected from the group consisting of: a genetic defect, cancer and retroviral infections, comprising administering to a subject in need thereof a therapeutically effective amount of a recombinant retroviral particle produced by transfecting a packaging cell line harboring at least one retroviral or recombinant retroviral construct coding for proteins required for said retroviral vector to be packaged, with a recombinant retroviral vector comprising, in operable linkage,

- retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- one or more coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: cecropin, prececropin, procecropin, a part thereof, an analogue thereof, a homologue thereof, and a combination thereof.

74. (New) The method according to Claim 73 for the treatment of human immunodeficiency virus infections comprising administering to a subject in need thereof a therapeutically effective amount of said recombinant retroviral particle wherein the coding sequence of said retroviral vector encodes for the amino acid sequence of cecropin or biologically active derivatives thereof.

75. (New) An isolated host cell infected with a virion according to Claim 62.

76. (New) A method for treatment of a cancer, comprising administering to a subject in need thereof a therapeutically effective amount of a recombinant retroviral particle produced by transfecting a packaging cell line harboring at least one retroviral or recombinant retroviral construct coding for proteins required for said retroviral vector to be packaged, with a recombinant retroviral vector comprising, in operable linkage,

- retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and

b) one or more coding sequences wherein at least one sequence encodes for a cecropin, or a cecropin analogue selected from the group consisting of, SB-37 and Shiva-1.

77. (New) A method for treatment of a viral infection, comprising administering to a subject in need thereof a therapeutically effective amount of a recombinant retroviral particle produced by transfecting a packaging cell line harboring at least one retroviral or recombinant retroviral construct coding for proteins required for said retroviral vector to be packaged, with a recombinant retroviral vector comprising, in operable linkage,

- a) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- b) one or more coding sequences wherein at least one sequence encodes for a cecropin, or a cecropin analogue selected from the group consisting of, SB-37 and Shiva-1.

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